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Small angle neutron scattering studies of non-ionic surfactant vesicles

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Small angle neutron scattering (SANS) studies have been carried out to establish the relationship between the molecular structures of a series of novel non-ionic surfactants, and the 3-dimensional structures of their corresponding vesicles. On the basis of results obtained, it was hoped that a more rational strategy could be followed in selecting the most appropriate members of this series to synthesize for use in the manufacture of drug delivery vehicles. The surfactants studied were members of the series, 1,2-di-alkyl-*O*-glyceryl-3-(ω-methoxy-polyoxyethylene), more conveniently summarised using the nomenclature $2C_nMPEG_m$, where n and m are respectively, the number of carbon atoms in each of the two alkyl chains, and the number of oxyethylene units in the polar head group.

Characterisation of the sonicated vesicle preparations by means of photon correlation spectroscopy showed that they were perfectly stable for periods up to 6 months, having mean hydrodynamic diameters of the order of 110±30nm.

For the SANS experiments (performed using the instrument D17 at the Institut Laue-Langevin), two batches of vesicle samples were prepared, dispersed either in D_2O or 0.9% D_2O saline (the latter intended as an approximation to human serum).

The SANS studies were carried out using the fully protonated surfactant vesicles formed from $2C_{16}MPEG_{12}$, $2C_{16}MPEG_{17}$, $2C_{18}MPEG_{12}$ and $2C_{18}MPEG_{17}$; and also for the D_2O suspensions of vesicles formed using the equimolar mixtures $2C_{16}E_{12}/2C_{16}E_{17}$ and $2C_{18}E_{12}/2C_{18}E_{17}$. In all cases, the measurements were carried out using samples with a total surfactant concentration of 2.5mg/mL.

Analyses of the SANS data were carried out treating the vesicle lamellae as infinite planar sheets (justified on the grounds of the large size of the vesicles and their low surface curvatures). The SANS curves of neutron intensity I(Q) vs. neutron momentum Q were accordingly transformed to give Guinier plots of $Ln(I(Q)*Q^2)$ vs.Q^2 (Kratky, 1963), where the linear portions of these curves in the low Q domain were used to determine the radius of gyration of the vesicle lamellae (Rg), and the corresponding second moment thicknesses of the lamellae (σ, obtained as $Rg\sqrt{12}$; see Table 1).

	Vesicle lamellae thicknesses (Å)	
Surfactant	D_2O	D_2O/NaCl
$2C_{16}MPEG_{12}$	96±9	75±1
$2C_{16}MPEG_{12}$	54±1	54±1
$2C_{16}MPEG_{12}$	110±8	ND
$2C_{16}MPEG_{12}$	65±6	66±1
$2C_{18}MPEG_{12}$/ $2C_{18}MPEG_{17}$	102±1	ND
$2C_{16}MPEG_{12}$/ $2C_{16}MPEG_{17}$	63±1	55±1

Table 1. Lamellae thicknesses for the different surfactant vesicles (ND=Not determined)

We note firstly that the lamellae thicknesses for the C_{18} chain surfactant vesicles are of the order of 50-60Å, whilst those for the C_{16} chain surfactant vesicles lie in the range 90-100Å. It is thus concluded that the C_{18} chain surfactant vesicles are delimited by single bilayer lamellae, and that the C_{16} chain surfactants form vesicles with twin-bilayer lamellae. In addition, it is seen that the lamellae thicknesses for the C_{18} chain surfactant vesicles are unaffected by the presence of salt in the suspending medium, whilst the $2C_{16}MPEG_{12}$ vesicles have lamellae that shrink in this environment.

The high in vitro stability of these surfactant vesicles makes them eminently suitable for use as drug delivery vehicles, and the surfactant $2C_{18}MPEG_{12}$ in particular looks promising because the integrity of its vesicles seems unlikely to be perturbed in human plasma following intravenous administration.

Kratky, O. (1963), Prog. Biophys. & Mol. Biol. **13** : 107-173